Synthetic Organic Chemistry - Fine Organic Synthesis -

Prof
FUJI, Kaoru
(D Pharm Sc)

Assoc Prof
KAWABATA, Takeo
(D Pharm Sc)

Instr
TSUBAKI, Kazunori
(D Pharm Sc)

Techn
TERADA, Tomoko

Guest Res Assoc
BAGUL, D. Trusar
(Ph D)

Guest Res Assoc
OZTURK, Orhan
(Ph D)

Students

MOMOSE, Yashima (D4)
NURUZZMAN, Mohammad (D3)
OHTSUBO, Tadamune (D2)
TANAKA, Hiroyuki (D1)
FUKAYA, Takayuki (M2)
KUSUMOTO, Tomokazu (M2)
KAWAKAMI, Shin-pei (M2)
MORIMOTO, Tatsuya (M2)
HIRASE, Keizo (M1)
MORIKAWA, Hiroshi (M1)
NAGAOKA, Yoshie (M1)

Scope of Research

The research interests of the laboratory include the development of new synthetic methodology, molecular recognition, and total synthesis of natural products. Programs are active in the areas of use of chiral leaving groups for an asymmetric induction, asymmetric alkylation of carbonyl compounds based on “memory of chirality”, development of new type of chiral nucleophilic catalysts, utilization of 8,8’-disubstituted 1,1’-binaphthyls as a chiral controller, visualization of molecular length by functionalized phenolphthalein, use of homooxacalixarene for molecular recognition, syntheses of molecular switch, structural and functional investigation of homo- and heterochiral oligomers.

Research Activities (Year 2001)

Presentations

Dynamic chirality of enolates: Memory of chirality in alkylation reactions, Kawabata T, Symposium on Chiral Molecular Science of 21st Century, 7 March.

Design and preparation of a new generation of chiral nucleophilic catalysts derived from 4-hydroxyproline, Kawabata T, Stragies R, et al., The 15st French-Japanese Synposium on Medicinal and Fine Chemistry, 8 May.

Sequence-selective visual recognition of non-protected dipeptides, Tsubaki K, Fuji K, et al., 26th International Symposium on Macrocyclic Chemistry, 15 July.

Asymmetric induction based on the dynamic chirality of enolates, Fuji K, 18th International Congress of Heterocyclic Chemistry, 30 July.

Enantioselective acceleration in kinetic resolution with a chiral nucleophilic catalyst, Kawabata T, Momose Y, Fuji K, et al., 18th International Congress of Heterocyclic Chemistry, 2 August.

Memory of chirality: A new principle in enolate chemistry, Fuji K, The First NIAF-Merinos- Joint Meeting on Basic and Applied Organic Synthesis, 1 October.

Asymmetric induction based on dynamic chirality of enolates: Direct asymmetric alkylation of α-amino acids, Kawabata, T, 32th Annual Meeting of Union of Chemistry, 5 October.

Grants

Kawabata T, Aymmetric synthesis through nucleophilic catalysis, Grant-in-Aid for Scientific Research (B) (2), 1 April 1999 - 31 March 2002.

Kawabata T, Dynamic control of stereochemistry, Grant-in-Aid for Scientific Research on Priority Areas No.706, 1 April 1998 - 31 March 2001.

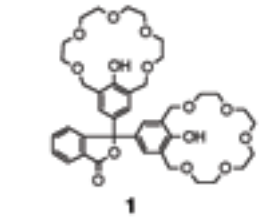
Fuji K, Construction of asymmetric environment by axially chiral molecules, Grant-in-Aid for Scientific Research (B) (2), 1 April 1998 - 31 March 2001.

Tsubaki K, Recognition and visualization of chirality by functionalized cyclic polyethers, Grant-in-Aid for Scientific Research Shorei A, 1 April 1999 - 31 March 2001.

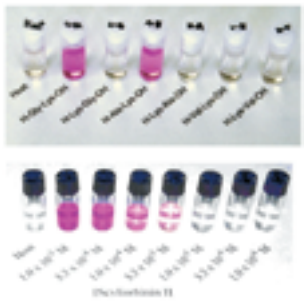
Topics

Sequence-specific coloration of dipeptides by functionalized phenolphthalein in aqueous media

Tracing the binding of host molecules with the guests by color change attracts scientists of many disciplines and is of great fun. We have found that a receptor **1** with phenolphthalein and two crown ethers in a molecule develops brilliant purple color in the presence of dipeptides with a specific amino acid-sequence containing lysine as a *C*-terminal. This type of color development could be extended to the detection of oligopeptides of a specific sequence at the *N*-terminal (Scyliorhinin I = H-Ala-Lys-Phe-Asp-Lys-Phe-Tyr-Gly-Leu-Met-NH_2). Advantage of this method includes that 1) the non-protected peptides can be used as a guest molecule and 2) detection leading to color development can be performed in the aqueous solution.



1



Total synthesis of a cell cycle regulator, spirotryprostatin B

Spirotryprostatin B (**2**), a potent antimitotic agent that was isolated from the fermentation broth of *Aspergillus fumigatus* has been shown to inhibit progression of the mammalian cell cycle in the G2/M phase at micromolar concentrations. Total synthesis of **2** was performed *via* asymmetric nitroolefination. Treatment of oxindole **3** with *n*-BuLi followed by **4** gave (*S*)-**5** in 97% ee, which was successfully transformed to **2**.

Enantioselective acceleration in kinetic resolution of racemic alcohols with a chiral nucleophilic catalyst

Development of an artificial low molecular-weight catalyst with enzymatic functions is a long-standing challenge of organic chemistry. A chiral nucleophilic catalyst **6** was developed to mimic the enantioselective acylating properties of enzyme such as lipase. Kinetic resolution of *racemic*-**7** was performed through acylation in the presence of 0.5 mol% of **6**. Enantiopure (1*R*, 2*S*)-**7** was recovered at 66% conversion. The selectivity factor {*s* = k(fast-reacting enantiomer / k(slow-reacting enantiomer)} is 17 at 20 °C and 54 at –40 °C. Kinetic study of the acylation and analysis of the reactive intermediate indicated that the discrimination of enantiomers by **6** is due to the specific acceleration of one enatiomer's reaction pathway, rather than the specific deceleration of the others'. This is in contrast to typical non-enzymatic catalysis. The observed enantioselective acceleration could be ascribed to the transition state hydrogen bonding between C(8)-OH of **6** and the carbonyl group of the fast-reacting enantiomer, (1*S*, 2*R*)-**7**.